Remarks

Rejections under 35 USC §112, 2nd paragraph

The Office Action rejected claim 33 as indefinite because the terms "mature sequence" and "extracellular domain" are allegedly not defined in the claim or the specification. Applicant respectfully traverses this rejection because it is incompatible with the examination principles discussed in the Manual of Patent Examining Procedure (MPEP).

In particular, MPEP §2173.02 sets forth a three-prong analysis for examining a claim for compliance with the definiteness requirement, stating that the "claim language *must be* analyzed, not in a vacuum, but in light of:

(A) The content of the particular application disclosure;

(B) The teachings of the prior art; and

(C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made." MPEP 2100-218 (Rev. 6, Sept. 2007) (emphasis added). Furthermore, MPEP §2173.02 states that if an Office action contains a rejection under 35 USC §112, then the Office action should include "an analysis as to why the phrase(s) used in the claim is 'vague and indefinite'". *Id.* at 2100-219.

It is not evident from the Office action that either of these principles was followed with respect to the examination of claim 33. The Office action does not discuss the teachings of the prior art and does not discuss what claim interpretation would be given by the skilled artisan. Rather, the Office action merely states that "the metes and bounds" of claim 33 can not be determined because the terms "mature sequence" and "extracellular domain" are not defined in the claim or the specification. Such a conclusory statement provides no explanation as to *why* these terms are indefinite under the three prong analysis mandated by MPEP §2173.02. Indeed, Applicant respectfully asserts an opposite conclusion is warranted when this three prong analysis is applied to these claim terms, as will be shown below.

Claim 33 is directed to a method of inhibiting IL-17C activity in a subject with psoriasis by administering to the subject a binding composition. This claim states that the binding composition (1) comprises an antigen binding site that binds to a human IL-17C protein that

comprises the mature sequence in SEQ ID NO:24 and (2) blocks binding of the IL-17C protein to the extracellular domain of a human IL-17RE protein. Claim 33 also states that the extracellular domain comprises amino acids 1-424 of SEQ ID NO:12.

Prior to the filing date of the application, IL-17C was known in the art as a member of the IL-17 cytokine family (see, e.g., Li et al., PNAS 97(2):773-778 (2000) (Cite No. AN in the Information Disclosure Statement submitted Dec. 29, 2003; Moseley, et al., *Cytokine & Growth Reviews* 14:155-174 (2003), Cite No. AQ in the Information Disclosure Statement submitted Dec. 29, 2003). Similarly, IL-17RE, which was also known as DCRS9, had been assigned to the IL-17 receptor family. *See*, e.g., Moseley, et al., (*supra*); and WO 01/90358 (Cite No. AZ in the Information Disclosure Statement submitted August 25, 2005). It was also known that there were several splice variants for IL-17RE. *See*, e.g., Moseley, et al., (*Id.* at p. 157-158); and WO2003/006609 at p. 8. Table 2 (Cite No. AE in the Information Disclosure Statement submitted Dec. 29, 2003).

The method recited in claim 33 is based, in part, on Applicant's discovery that IL-17C is a ligand for IL-17RE. The application teaches in Example III on pages 55-56 that the identification of IL-17C as a ligand for IL-17RE was made by incubating various FLAG-tagged IL-17 ligands with cells expressing various IL-17 chimeric receptors and seeing which ligands bound to which receptors. Each FLAG-tagged IL-17 ligand was prepared by subcloning its *mature coding sequence* (e.g., the mature coding sequence of IL-17C) into the pCMV vector (see paragraph [0167] on p. 55), while each IL-17 chimeric receptor was made by "subcloning the extracellular domain to the transmembrane and intracellular domains of murine GCSFR in the vector pMX-puromycin" (see paragraph [0168] on p. 56). Thus, it would be evident to the skilled artisan from reading the specification that the binding interaction to be blocked in the claimed method is between the mature IL-17C protein and the extracellular domain of IL-17RE. The application teaches that the amino acid sequence for IL-17C is SEQ ID NO:24, which contains 197 amino acids and that the amino acid sequence for IL-17RE is SEQ ID NO:12 (see, e.g., paragraph [0010] on p. 4).

Although the application does not *specifically* state what portion of SEQ ID NO:24 is the *mature sequence* of IL-17C, there was no need to as this information was readily available in the

prior art. *See*, e.g., Li et al., *supra* (Figure 1 on p. 774); US Patent No. 6,569,645 (column 18, lines 20-24 and Figure 30); WO 99/60127 (p. 13, lines 3-9; p. 15, lines 19-23 and Figure 7A; Cite No. BJ in the Supplemental Information Disclosure Statement submitted herewith).

Similarly, there was no need to explicitly define the term "extracellular domain of a human IL-17RE protein" in the application, as its meaning was readily discernible from the prior art. For example, it was already known that members of the IL-17 receptor family are single-pass transmembrane proteins with an extracellular ligand-binding domain at the amino terminus, a transmembrane domain, and a cytoplasmic tail. *See*, e.g., Moselely et al., (*Id.* at p. 157, 2nd column, lines 1-2); WO 96/29408 (p. 3, lines 23-31; Cite No. AA in Information Disclosure Statement submitted Dec. 29, 2003); and WO 01/46420 (p. 21, lines 1-10 and Examples 21-22 on p. 125-129). Moreover, claim 33 even explicitly states which amino acids are located in the extracellular domain of the human IL-17RE receptor to which the IL-17C ligand would bind.

In conclusion, when the teaching of the present application is considered in light of what was known in the prior art, Applicant respectfully asserts that, as of the filing date of the present application, the skilled artisan could have readily discerned the meaning of the terms "mature sequence in IL-17C" and "extracellular domain of the human IL-17RE protein" with reasonable certainty. Thus, a rejection of claim 33 under Section 112, second paragraph for indefiniteness is not warranted and should be withdrawn.

The Office Action also rejected Claim 34 as indefinite because it depended from a cancelled claim. Applicant respectfully requests withdrawal of this rejection in view of the foregoing amendment to claim 34, which now depends from claim 33.

Rejection Over Prior Art

Claims 33-35 stand finally rejected under 35 U.S.C. §102(a) as being anticipated by Chen et al. (US 6,569,645). The Office Action alleges that Chen et al. teach the use of antibodies that inhibit IL-17C activity for the treatment of psoriasis, and cites to several disconnected passages within that patent as support for this allegation. Applicant respectfully submits that Chen et al. do not anticipate the present claims because Chen et al. do not adequately describe or enable the use of such antibodies to treat psoriasis for the following reasons.

Chen et al. describe 5 "new" members of the IL-17 cytokine family and 4 "new" members of the IL-17 receptor family, and disclose some *in vitro* activity data and expression data for some of these family members, including IL-17C. When discussing specific diseases that could be treated using these cytokine and receptor proteins, as well as agonists or antagonists thereof, Chen et al., typically refer to all of the IL-17 cytokine and receptor family members as PRO polypeptides, with limited exceptions. None of these exceptions explicitly teach treating psoriasis using an antagonist of IL-17C, let alone an antibody antagonist. Thus, such generic passages, which include those cited in the Office Action, do not clearly and unambiguously disclose use of antibodies that inhibit IL-17C to treat psoriasis.

For example, while psoriasis is mentioned in column 92, lines 63-66 and column 96, lines 54-55 as stated in the Office Action, the full text of these passages generically refer to all IL-17 cytokine and receptor polypeptides and to all antibodies to these polypeptides for treating any one of a laundry list of diseases:

> O. Methods of Treatment
>
> It is contemplated that the *polypeptides, antibodies and other active compounds of the present invention may be used to treat various immune related diseases and conditions*, such as T cell mediated diseases, including those characterized by infiltration of inflammatory cells into a tissue, stimulation of T-cell proliferation, inhibition of T-cell proliferation, increased or decreased vascular permeability or the inhibition thereof.
>
> Exemplary conditions or disorders to be treated with the *polypeptides, antibodies and other compounds of the invention*, include, but are not limited to systemic lupus erythematosis, rheumatoid arthritis, juvenile chronic arthritis, osteoarthritis, spondyloarthropathies, systemic sclerosis (scleroderma), idiopathic inflammatory myopathies (dermatomyositis, polymyositis), Sjoegren's syndrome, systemic vasculitis, sarcoidosis, autoimmune hemolytic anemia (immune pancytopenia, paroxysmal nocturnal hemoglobinuria), autoimmune thrombocytopenia (idiopathic thrombocytopenic purpura, immune-mediated

thrombocytopenia), thyroiditis (Grave's disease, Hashimoto's thyroiditis, juvenile lymphocytic thyroiditis, atrophic thyroiditis), diabetes mellitus, immune-mediated renal disease (glomerulonephritis, tubulointerstitial nephritis), demyelinating diseases of the central and peripheral nervous systems such as multiple sclerosis, idiopathic demyelinating polyneuropathy or Guillain-Barré syndrome, and chronic inflammatory demyelinating polyneuropathy, hepatobiliary diseases such as infectious hepatitis (hepatitis A, B, C, D, E and other non-hepatotropic viruses), autoimmune chronic active hepatitis, primary biliary cirrhosis, granulomatous hepatitis, and sclerosing cholangitis, inflammatory bowel disease (ulcerative colitis: Crohn's disease), gluten-sensitive enteropathy, and Whipple's disease, autoimmune or immune-mediated skin diseases including bullous skin diseases, erythema multiforme and contact dermatitis, *psoriasis*, allergic diseases such as asthma, allergic rhinitis, atopic dermatitis, food hypersensitivity and urticaria, immunologic diseases of the lung such as eosinophilic pneumonias, idiopathic pulmonary fibrosis and hypersensitivity pneumonitis, transplantation associated diseases including graft rejection and graft-versus-host-disease.

US 6,569,645, column 92, line 62 to column 93, line 36, emphasis added.

Chen et al. also discuss the treatment of psoriasis in the Summary of the Invention, where they are equally ambiguous:

> In another embodiment, the invention concerns a method of treating an immune related disorder in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of *a PRO polypeptide, an agonist thereof, or an antagonist thereto*. In a preferred aspect, the immune related disorder is selected form the group consisting of: systemic lupus erythematosis, rheumatoid arthritis, osteoarthritis, juvenile chronic arthritis, spondyloarthropathies, systemic sclerosis, idiopathic inflammatory myopathies, Sjoegren's syndrome, systemic vasculitis, sarcoidosis, autoimmune hemolytic anemia, autoimmune thrombocytopenia, thyroiditis, diabetes mellitus, immune-

mediated renal disease, demyelinating diseases of the central and peripheral nervous systems such as multiple sclerosis, idiopathic demyelinating polyneuropathy or Guillain-Barré syndrome, and chronic inflammatory demyelinating polyneuropathy, hepatobiliary diseases such as infectious, autoimmune chronic active hepatitis, primary biliary cirrhosis, granulomatous hepatitis, and sclerosing cholangitis, inflammatory bowel disease, gluten-sensitive enteropathy, and Whipple's disease, autoimmune or immune-mediated skin diseases including bullous skin diseases, erythema multiforme and contact dermatitis, *psoriasis*, allergic diseases such as asthma, allergic rhinitis, atopic dermatitis, food hypersensitivity and urticaria, immunologic diseases of the lung such as eosinophilic pneumonias, idiopathic pulmonary fibrosis and hypersensitivity pneumonitis, transplantation associated diseases including graft rejection and graft-versus-host-disease.

US 6,569,645, column 6, lines 8-35, emphasis added.

The above quoted passages represent a staggering number of permutations of potentially therapeutic compounds and diseases; thus, there is no way for the skilled artisan reading these passages to see any clear teaching of which "compound of the invention" would be useful to treat which immune-related disease, let alone a clear teaching of treating psoriasis using antibodies that inhibit IL-17C.

The remainder of the Chen et al. disclosure only exacerbates the ambiguity of the above cited passages. For example, while Chen et al. teach that IL-17 "*may* contribute to" psoriasis, they also teach that IL-17 and IL-17C have "differential" activities (column 124, line 35). Also, in contrast to the present application, Chen et al. do not disclose expression of IL-17C in *any* disease tissue, let alone elevated expression of IL-17C in psoriasis skin as compared to normal skin. Indeed, at column 134, lines 37-43, Chen et al. admit that they don't know which inflammatory conditions may be treated with IL-17C antagonists:

> Finally, it is well known that growth factors can have biphasic effects and that diseased tissue can respond differently than normal tissue to a given factor in

vivo. For these reasons, *antagonists or agonists* (e.g., the proteins themselves) of IL-17B (PRO1031), *IL-17C (PRO1122)*, or IL-17, may be useful for the treatment of *inflammatory conditions* and joint disorders such as arthritis.

US 6,569,645, column 134, lines 37-43, emphasis added.

Thus, since Chen et al. explicitly teach that psoriasis is an inflammatory disease (column 96, lines 54-55), but that they do not even know whether an agonist or an antagonist of IL-17C would be useful for treating any particular inflammatory condition, let alone psoriasis, this prior art document can not constitute an adequate description of using an antibody that inhibits IL-17C to treat psoriasis. Moreover, due to the long list of "immune-related" diseases mentioned in the application for which any of the IL-17 cytokine family members, or any of the IL-17 family receptors, or any agonists thereof, or any antagonists thereof, "may be used to treat" (US 6,569,645, column 92, line 62 to column 93, line 36), Chen et al fail to enable a method of using an antibody that inhibits IL-17C to treat psoriasis as it would constitute undue experimentation to determine which of these compounds would be useful to treat which of these diseases.

In conclusion, because Chen et al do not provide an enabling description of using an antibody that inhibits IL-17C to treat psoriasis, this reference does not anticipate the present claims, and Applicant requests reconsideration and withdrawal of the anticipation rejection under 102(a). For the avoidance of doubt, Applicant continues to believe that Chen et al also do not explicitly or inherently describe antibodies that block binding of mature IL-17C to the extracellular domain of IL-17RE and do not enable making such antibodies.

Applicant respectfully submits that the claims are in condition for allowance. If the undersigned can be of any assistance to the Examiner in addressing issues to advance the application to allowance, please contact Applicant's attorney at the number set forth below.

Respectfully submitted,

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